A2 cont'd

Claim 24. (NEW) The method of claim 3, wherein the promoter gene sequences are selected from the group consisting of AG, AGL5, Bcp1, LAT52, PLENA, SIM, avrRpt2, and alc.

REMARKS

Applicants have amended Claim 1, and new claims have been added to conform with the suggestions provided in the Action. Support for new claims 7 and 8, as well as for the amendment to Claim 1, is found in the claims as filed, and throughout the specification. Consequently, no new matter has been added by virtue of these changes and their entry is respectfully requested.

The Action has rejected Claims 1-6 under 35 U.S.C. 112, second paragraph as allegedly being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

Applicants respectfully traverse.

Applicants have amended the claims as suggested in the Action; for example, "creation" has been amended to "production." In view thereof, reconsideration and withdrawal of the objection is requested.

Applicants further disagree with the allegation set forth in the Action that the term, "transiently transgenic plant," is unclear. The invention teaches the production of a plant that is transgenic, *i.e.* comprises a heterologous gene functionally coding for a desired phenotypic trait, but is only "transiently transgenic" in that the nucleic acid comprising the heterologous gene is **excised** from the genome of the plant at the time and under predetermined environmental and/or developmental conditions (after expression of the gene has conferred the desirable phenotypic trait). Therefore, the plant that was rendered transgenic by transformation with nucleic acid comprising the gene of interest **is no longer transgenic**, *i.e.*, the plant is "transiently transgenic," as the genome of the plant no longer contains the heterologous nucleic acid comprising the gene of interest,

and the plant reverts to a genomic type functionally indistinguishable from the wild type genome as it existed prior to transformation with the heterologous nucleic acid. (See, for example, page 9, paragraph 17). The invention provides "a gene cassette for the **reversible introduction** of heterologous DNA sequences into the genome of a vegetatively propagated plant," (emphasis added). Since applicant's invention logically teaches production of a "transiently transgenic plant," applicants choose to describe the transient nature of the plant as a "transiently transgenic plant."

Quoting MPEP § 21110.02 in pertinent part:

> Applicant may be his or her own lexicographer as long as the meaning assigned to the term is not repugnant to the term's well known usage. *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). Any special meaning assigned to a term "must be sufficiently clear in the specification that any departure from common usage would be so understood by a person of experience in the field of the invention." *Multiform Dessicants Inc. v. Medzam Ltd.*, 133 F.3d 1473, 1477 45 USPQ2d 1429, 1432 (Federal. Cir. 1998).

In view thereof, reconsideration and withdrawal of the objections is requested.

The Action further alleges that the term "gene" is unclear. In response, Applicants point to page 17 of the application, paragraph 37, lines 16-28, whereby the term "gene," as taught by the invention, is described. However, for purposes of expedited examination, the claims have been amended to refer to "DNA sequences." In view thereof, reconsideration and withdrawal of the objection is requested.

Applicants have amended the terms "the recombinase-type protein," "the heterologous DNA," and "the promoter" in the claims to provide sufficient antecedent basis. Applicants further submit that a recombinase-type protein is fully described throughout the specification. See, for example, page 11, paragraph 21, lines 15-19 (examples of recombinase type proteins); page 18, paragraphs 39 and 40, lines 9-22 (illustrative example of a recombinase system and its recombinase-type protein). Thus, recombinase-type protein is well defined. Further, "DNA excision sequences" are also

defined throughout the specification. For example, page 10, paragraph 19, lines 14-29 define excision sequences as being "recognized only by the recombinase protein" which is why these sequences differ from non-excision sequences; see also page 18, paragraphs 39 and 40, lines 9-22 (illustrative example of specific excision sequence, *e.g.* loxP identified by SEQ ID NO: 1).

Applicants have amended Claim 1 for clarification. Applicants describe the various embodiments on pages 9, beginning of paragraph 17 through to page 13 up to the last sentence of paragraph 28. As disclosed in the specification, the excision sequences in the cassette flank the DNA sequence of interest, *i.e.* on the 5' and 3' ends of the sequence. The DNA sequences encoding for the recombinase-type protein can be positioned either 5' and/or 3' to the excision sequences. One of ordinary skill in the art recognizes that it is the recombinase protein that cleaves the excision sequences and therefore can be placed upstream or downstream, *i.e.* 5' or 3' to the excision sequences. Therefore, when the transiently activated promoter is activated and the recombinase protein is expressed, the recombinase protein cleaves the excision sequences flanking the heterologous gene of interest, thereby resulting in the excision of the heterologous DNA.

In view thereof, reconsideration and withdrawal of the objections is requested.

The action has also rejected Claims 1-6 under 35 U.S.C. 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention."

Applicants respectfully traverse.

The Action alleges that the "generation of a given particular phenotype is unpredictable" and bases the allegations on cited art that is not proper. References cited by the Examiner to allege that "gene expression levels and inheritance are unpredictable" include, Deroles *et al.*, **1988**, *Plant Mol. Biol.* 11:355-364; Dunwell *et al.*, **1990**, *Outlook*

on Agriculture; and Finnegan *et al. Bio/Tech.*, **1994**, 12:883-888. These references are not even current as of the date of the filing of the instant application, since these references were published as early as 1988 – at least 12 years prior to the instant application and, therefore, not reflective of the state of relevant knowledge as of the time of filing of the instant application. Even if these older references and the references published after the instant application (Gidoni *et al.* 2000; Gidoni *et al.* 2001) were applicable, they do not have any bearing on the present application as these references teach the transmission rates of transgenes in progeny based on Mendelian genetics. In contrast, Applicants teach methods for excision of transgenes in a parent plant so the phenotype of the plant reverts to a wild type plant. Thus, applicants teach **removal** of a heterologous sequence and not transmission of that sequence into progeny plants. In view thereof, reconsideration and withdrawal of the rejection is requested.

"Breadth of the claims." Applicants have amended the claims and added new claims to expedite examination.

The Action states an objection to the specification for, allegedly, not having "working examples." The Examiner alleges that the "prophetic examples" do not provide guidance nor specific details. Such a basis for rejection of the claims is improper. See, for instance, the Manual of Patent Examining Procedure at § 2164.02, which states:

> "Compliance with the enablement requirement of 35 U.S.C § 112, first paragraph does not turn on whether an example is disclosed. An example may be 'working' or 'prophetic'."
>
> "An applicant need not have actually reduced the invention to practice prior to filing (*Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987)."

Therefore, the Action's rejection based on "specific details, "results of the use of various systems," are improper. However, Applicants have described appropriate vectors (page 16, paragraph 35); transformation techniques (pages 15-16, paragraph 34); distinguishing genes and traits (paragraph 37, page 17); recombinase-type proteins and

systems (page 17, paragraph 38 through to page 19, paragraph 42); marker genes (page 21 paragraphs 47 and 48); and controlled expression (page 21, paragraph 49 through to page 22, paragraph 50). One of ordinary skill in the art would not require undue experimentation to achieve "specific results," nor are the applicants required to "optimize" and provide specific "expression patterns," "stability of transgenes through generations," especially so when applicants are not desirous of obtaining generations of transgenic plants. Furthermore, absolutely no evidence has been presented in the Action to establish why one skilled in the art could not make and use the claimed subject matter based on Applicants' disclosure. Such a basis for rejection under § 112, ¶ 1 is simply not proper. It is well established that in the absence of any evidence why a supporting disclosure is not sufficient, the mere allegation of inadequacy is not considered to constitute a satisfactory basis for rejection under § 112, ¶ 1. See, for instance, the Manual of Examining Procedure at Section 2164.04 which states (quoting *In re Marzocchi*):

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

In view thereof, reconsideration and withdrawal of the rejection are requested.

The Action has also rejected Claims 1-6 under 35 U.S.C. 102(b) as allegedly being anticipated by Oliver *et al.*, US 5,723,765, issued March 3, 1998.

Applicants respectfully traverse.

Oliver *et al.* teach a method wherein:

> [a] gene whose expression results in an altered plant phenotype which is linked to the transiently-active promoter through a blocking sequence separating the transiently-active promoter and the gene, unique specific excision sequences flanking the blocking sequence, wherein the specific excision

> sequences are recognizable by a site-specific recombinase, a gene encoding the site-specific recombinase, an alternative repressible promoter linked to the recombinase gene, and an alternative gene that encodes the repressor specific for the repressible promoter, the action of the repressor being responsive to an applied or exogenous stimulus. (col. 3, lines 1-15; emphasis added).

Oliver *et al.* therefore do not teach excision of the gene that confers the trait desired, but teaches the use of a blocking sequence that inhibits expression of a gene. The gene that produces the transgenic phenotype is **never** excised and the transgenic gene **remains** in the transgenic plant to be passed on to progeny. In many ways, the system taught by Oliver *et al.* is merely a way to "turn on" a gene transformed into a plant; in no way do the teachings of Oliver *et al.* suggest that it is possible, after expression of the transgene, to return the plant to its wild-type state. Furthermore, the cited reference also teaches that many steps are required to obtain the desired phenotype, *e.g.*, expression of the heterologous transgene is suppressed by an inhibitor which is under the control of a repressor, which in turn is controlled by a repressor promoter, which in turn is responsive to external stimuli.

In contrast, Applicants teach a method of producing a plant that can express a desired phenotype by expression of a desired DNA sequence and a method of excising that sequence so the sequence does **not** remain in the plant thereby, preventing the propagation of transgenic plants. Furthermore, applicants accomplish this using only a transiently activated promoter, a recombinase gene and the specific excision sequences flanking the heterologous DNA. Oliver *et al.* does not anticipate or teach deletion of a heterologous transgene to revert to a wild type.

In view thereof, reconsideration and withdrawal of the rejection is requested.

CONCLUSION

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,

Daniel F. Coughlin (Reg. No. 36111)
EDWARDS & ANGELL, LLP
Three Stamford Plaza
301 Tresser Blvd., Suite 1310
Stamford, CT 06901-3239